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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/734,527	12/12/2003	Richard Wisdom	2002DE315	9703
7590	05/02/2006			
			EXAMINER	
			GOUGH, TIFFANY MAUREEN	
		ART UNIT	PAPER NUMBER	
		1651		

DATE MAILED: 05/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/734,527	WISDOM, RICHARD	
	Examiner Tiffany M. Gough	Art Unit 1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on ____.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-9 is/are pending in the application.
 - 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) Claim(s) ____ is/are allowed.
- 6) Claim(s) 1-9 is/are rejected.
- 7) Claim(s) ____ is/are objected to.
- 8) Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on ____ is/are: a) accepted or b) objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. ____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>6/7/2004</u> . | 6) <input type="checkbox"/> Other: ____ . |

DETAILED ACTION

Specification

The use of the trademark Chirazyme® has been noted in this application.

It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear in claim 1, therefore all dependent claims, how the term "suitable" may differentiate one ester from another and to what degree an ester would be considered "suitable".

If a dependent claims fails to remedy or clarify the deficiencies of the independent claim subjected to a 35 U.S.C. 112, second paragraph rejection, then such dependent claims are also rejected under 35 U.S.C. 112, second paragraph

The term "low" in claim 4 is a relative term, which renders the claim indefinite. The term "low" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 7 contains the trademark/trade name Lipase QL, Lipase QLM, and Chirazyme L-10. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a hydrolytic enzyme and, accordingly, the identification/description is indefinite.

Claim 8 is indefinite in that the abbreviation "ee" is not defined and may therefore have alternative interpretations, such as enzyme excess, and may be interpreted to mean something which is not intended. In addition, if an industrial definition exists, the understanding of "ee" can change over time and therefore may possess the same meaning it possess today.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1,2,4-6 and 8 rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Ghorpade et al (Tetrahedron: Asymmetry, 1999, vol 10, pg. 891-899).

II. A REJECTION UNDER 35 U.S.C. 102/103 CAN BE MADE WHEN THE PRIOR ART PRODUCT SEEMS TO BE IDENTICAL EXCEPT THAT THE PRIOR ART IS SILENT AS TO AN INHERENT CHARACTERISTIC

Where applicant claims a composition in terms of a function, property or characteristic and the composition of the prior art is the same as that of the claim but the function is not explicitly disclosed by the reference, the examiner may make a rejection under both 35 U.S.C. 102 and 103, expressed as a 102/103 rejection. "There is nothing inconsistent in concurrent rejections for obviousness under 35 U.S.C. 103 and for anticipation under 35 U.S.C. 102." In re Best, 562 F.2d 1252, 1255 n.4, 195 USPQ 430, 433 n.4 (CCPA 1977). This same rationale should also apply to product, apparatus, and process claims claimed in terms of function, property or characteristic. Therefore, a 35 U.S.C. 102/103 rejection is appropriate for these types of claims as well as for composition claims.

Applicant claims a process for the preparation of (1S,4R)-4-hydroxycycloent-2-enyl esters by reacting a cis-cyclopent-1-ene-diol, or racemic or partially resolved 4-hydroxycyclopent-3-enyl ester with an ester donor in the presence of an *Alcaligenes* sp. lipase. The reaction is carried out within a temperature range of 10°C to room temperature in a ketone solvent such as acetone,

isobutylmethylketone or methylethylketone and containing an ester donor such as vinyl acetate or vinyl propionate. Applicant claims an ee (enantiomeric excess) of >95%.

Ghorpade et al disclose a lipase/esterase catalyzed desymmetrization of meso-cyclopenten-1,4-diol by transesterification using Chirazyme®. Transesterification of the meso-diol was carried out utilizing vinyl acetate as an acyl donor in various organic solvents including acetone (see pg. 892, 2.1 section) at temperatures ranging from 0°C to room temperature (see Table 3) with >60% yield and >98% ee (see p. 897 Conclusion section).

The functionality of organic compounds such as 1,4 or 3,5-diols are analogous. Therefore, positional isomers inherently possess the same functionality and would react in a transesterification reaction in a similar manner to achieve an ester product.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ghorpade et al (Tetrahedron: Asymmetry, 1999, vol 10, pg. 891-899) in view of Kurozumi et al (U.S. Patent 4,008,125, 1977) and Minai et al (U.S. Patent 5,191,109, 1993)

Applicant claims a process for the preparation of (1S,4R)-4-hydroxycycloent-2-enyl esters by reacting a cis-cyclopent-1-ene-3,5-diol, or racemic or partially resolved 4-hydroxycyclopent-3-enyl ester with an ester donor in the presence of an *Alcaligenes* sp. lipase, either in free form or immobilized on a carrier. Further, recovering by filtration and purifying the product by stripping the solvent, resuspending the oil in an aqueous solution and extraction into an alkane solvent. The reaction is carried out within a temperature range of 10°C to room temperature in a ketone solvent such as acetone, isobutylmethylketone or methylethylketone and containing an ester donor such as vinyl acetate or vinyl propionate. Applicant further claims that the lipase be either Lipase QL, Lipase QLM, or Chirazyme®, or a purified or immobilized derivative. Applicant claims an ee (enantiomeric excess) of >95%.

Ghorpade et al disclose a lipase/esterase catalyzed desymmetrization of meso-cyclopenten-1,4-diol by transesterification using Chirazyme®. Transesterification of the meso-diol was carried out utilizing vinyl acetate as an acyl donor in various organic solvents including acetone (see pg. 892, 2.1 section) at temperatures ranging from 0°C to room temperature (see Table 3) with >60% yield and >98% ee (see p. 897 Conclusion section). Further, recovery was obtained by filtering, evaporating, and extracting with ethyl acetate/petroleum ether to elute product (see p.898 section 4.2).

Ghorpade differs from the claims in that the starting product is not a 3,5-diol. However, one of ordinary skill in the art would have a reasonable

expectation of success in obtaining an ester product ,as claimed by applicant and Ghorpade, using the starting disclosed by Ghorpade. A 1,4-diol is simply a position isomer of the 3,5-diol claimed by applicant which is reacted with a hydrolytic enzyme to produce an ester, specifically a desirable acetate product which is used to synthesize products such as prostaglandins. Given the claim to a process for preparing an ester, one would expect success in obtaining an ester product after resolving such alcohol or ester with an enzyme such as lipase when using either a 1,4 or 3,5-diol substrate. The functionality of the organic compounds are analogous, whether it is a 1,4 or 3,5-diol. See MPEP 2144.09

MPEP 2144.09 Close Structural Similarity Between Chemical Compounds (Homologs, Analogues, Isomers)

REJECTION BASED ON CLOSE STRUCTURAL SIMILARITY IS FOUNDED ON THE EXPECTATION THAT COMPOUNDS SIMILAR IN STRUCTURE WILL HAVE SIMILAR PROPERTIES

A prima facie case of obviousness may be made when chemical compounds have very close structural similarities and similar utilities. "An obviousness rejection based on similarity in chemical structure and function entails the motivation of one skilled in the art to make a claimed compound, in the expectation that compounds similar in structure will have similar properties." In re Payne, 606 F.2d 303, 313, 203 USPQ 245, 254 (CCPA 1979). See In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (discussed in more detail below) and In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991) (discussed below and in MPEP § 2144) for an extensive review of the case law pertaining to obviousness based on close structural similarity of chemical compounds.

See also MPEP § 2144.08, paragraph II.A.4.(c).

HOMOLOGY AND ISOMERISM ARE FACTS WHICH MUST BE CONSIDERED WITH ALL OTHER RELEVANT FACTS IN DETERMINING OBVIOUSNESS

Compounds which are position isomers (compounds having the same radicals in physically different positions on the same nucleus) or homologs (compounds differing regularly by the successive addition of the same chemical group, e.g., by -CH₂- groups) are generally of sufficiently close structural similarity that there is a presumed expectation that such compounds possess

similar properties. In re Wilder, 563 F.2d 457, 195 USPQ 426 (CCPA 1977). See also In re May, 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers prima facie obvious).

Further, Kurozumi et al. teach a process for preparing acyl esters of cyclopentene-diols, specifically cyclopent-1-en-3,5-diols which are reacted with a microorganism or a hydrolytic enzyme, i.e. a lipase or esterase (which may be supported on a carrier material, i.e. immobilized enzymes, see col.10, lines 61-66) to produce esters such as 4-hydroxycyclopent-2-en-1-one, such reaction is carried out at temperatures between 25-45°C . The product is isolated by either extraction with an organic solvent , such as acetate, benzene, ether, chloroform, or hexane followed by removal of the solvent by evaporation or separation by chromatography. However, the preferred method of product recovery is by salting out and continuous extraction (see column 10, lines 30-49). Kurozumi et al. further teach a diacyl ester containing either a cyclopent-1-en-3,5-diol and/or a trans-diester can be subjected to either a microorganism or enzyme having a selectivity in the hydrolysis rate between the acyloxy group of (R) and (S) configuration to accumulate at least one diester as an ester or diol by selectively hydrolyzing the diester and separating and recovering at least one hydrolyzed (R) and (S) (see column 4, lines 6-21). These compounds are valuable when used as starting materials for the preparation of prostaglandins or its analogues (see abstract) .

Therefore one would have a reasonable expectation of success and would further be motivated in using such reactants in the process as claimed by applicant and Ghorpade to obtain a desirable ester/acetate product.

Ghorpade also differs from the claims in that the enzyme Chirazyme® does not disclose its origin. However, Chirazyme® is a hydrolytic enzyme, which originates from a variety of organisms such as *Candida*, *Pseudomonas*, *Humicola*, *Alcaligenes* sp.(see "Supporting Information Table S I.) and further support is provided by Minai et al. (U.S. Patent 5,191,109). Minai et al disclose a process for preparing active 4-hydroxycyclopentenones , which are useful for preparing pharmaceutically active prostaglandins and intermediates for active and/or racemic 4-hydroxycyclopentenones. The pentenones are prepared by hydrolyzing cyclopentenone esters with an esterase including a lipase. The microorganisms from which such lipase and/or esterase is produced includes *Alcaligenes* and they further disclose the use of Lipase PL derived from *Alcaligenes* , manufactured by Meito Sangyo K.K (column 5, lines 8-13 and 45-48), further the enzymes disclosed by Minai et al. may be immobilized (see col.5,lines 65-68). The hydrolysis reaction may be carried out in a conventional buffer. In addition to the buffer, an inert solvent such as methyl isobutyl ketone, toluene or chloroform (see col. 6, lines 23-27). The desired product is isolated and separated from the esters by extracting the reaction mixture with a solvent (a ketone, acetate, or ether) distilling the extract and purifying by such means as column chromatography (see col.6, lines 35-42), conventional methods are also suitable such as extraction, liquid separation, concentration, and recrystallization

(col.7, lines 51-59). The reaction is carried out at a temperature within the range of -20 to 90° C.

One of ordinary skill in the art would therefore have been motivated to substitute the *Alcaligenes* sp. derived lipase disclosed by Minai for the Chirazyme or lipase disclosed by Ghorpade and/or Kurozumi in the process to produce esters ,based on the disclosure that lipases produced by *Alcaligenes* are successful in hydrolyzing such esters or alcohols such as those disclosed by Ghorpade and/or Kurozumi.

Therefore, the claimed invention as a whole is *prima facie* obvious over the art.

Conclusion

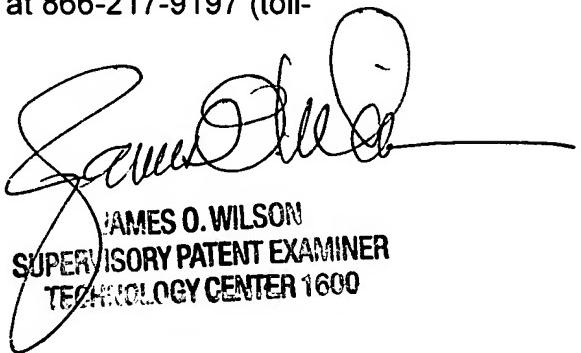
No claims are found allowable over the art.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tiffany M. Gough whose telephone number is 571-272-0697. The examiner can normally be reached on M-F 8-5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Tiffany Gough



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